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A convenient method to access long-chain and functionalised mixed methylphosphonate esters and their application in the synthesis of ionic liquids†

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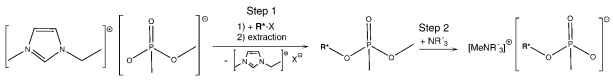
A new method to synthesise long-chain and functionalised methylphosphonate esters and the corresponding ionic liquids is reported. The synthesis comprises the formation of dialkyl methylphosphonate esters in a S_N2 reaction followed by the use of these esters as alkylating agents to form the corresponding, new alkyl methylphosphonate ILs.

During the last decade, great attention was paid to the synthesis and application of functionalised ionic liquids for distinct purposes, referred to as "task-specific" ionic liquids.[1–3] The most traditional concept for the synthesis of such functionalised ionic liquids involves the alkylation of amines or phosphine using alkylation agents carrying, *e.g.* amino, nitrile, hydroxy, halide, thiol or ester groups. This procedure directly yields ionic liquids with functionalised cations.[2] For the incorporation of functional groups into the IL's anion an approach of similar generality does not exist as only a few anions suitable for forming low melting salts accomodate alkyl chains that could carry suitable functionalised groups. Among these, alkylsulfate,[4] alkylsulfonate,[5] dialkylphosphate[6] and alkyl alkylphosphonate[7] ionic liquids are the most interesting candidates from a practical point of view. These classes of ionic liquids have found many interesting applications (*e.g.* separation technologies,[9] catalysis,[9] biomass treatment,[10] lubrication[11]) due to their industrial accessibility and their interesting physico-chemical properties. It is obvious that these classes of anions could further benefit from additional ionic liquid functionalities.

Up to now, only for ionic liquids with alkyl sulfate anions a straightforward synthetic methodology is known that gives access to a large range of compounds with different chain lengths and functionalities.[4] The established method starts from the methylsulfate or ethylsulfate salt and involves an acid catalysed transesterification reaction with any longer chain or functionalised alcohol. For alkylsulfonate ionic liquids dedicated routes to synthesise aminopropylsulfonates/aminobutylsulfonates[12] or halogen-propylsulfonate/halogenbutylsulfonate[13] have been described by reaction of amines or halide salts with the respective sultone. For dialkylphosphate ionic liquids the research is dominated by non-functionalised, short-chain alkyl groups with dimethylphosphates, diethylphosphates and dibutylphosphates being described in more detail.[7]



Scheme 1 Synthetic strategy applied in this work to synthesize functionalised alkyl methylphosphonate ionic liquids from [EMIM][(Me(Me)PO_3].

To the best of our knowledge, the structural anion variability of phosphonate ionic liquids has been restricted to date to methyl phosphonates ($[Me(H)PO_3]^-$)[8] and methyl methylphosphonates ($[Me(Me)PO_3]^-$). [EMIM][Me(H)PO_3] and [EMIM][Me(Me)PO_3] have been synthesised and applied in the context of HPLC applications,[14] biomass treatment[7] and glucose dehydrogenation.[15]

In this publication we report a new and very convenient method to synthesise mixed and functionalised phosphonate esters of the general type R*Me(Me)PO_3 (R* = functionalised alkyl group) that are isolated and later reacted as alkylating agents with methyl- or ethylimidazole to form a variety of new functionalised ionic liquids of the general type [cation][R*(Me)PO_3] (Scheme 1).

As shown in Scheme 1, the starting point of our research was the ionic liquid [EMIM][Me(Me)PO_3] that is readily obtained following literature procedures[14a] by the solvent-free reaction of ethylimidazole and dimethyl methylphosphonate (Me_2(Me)PO_3) at 100 °C. In our research we made the surprising observation that the $[Me(Me)PO_3]^-$ ion exhibits a nucleophilicity high enough to react in a S_N2-type substitution reaction with a variety of different, functionalised alkylating agents R*–X. The products of this anion transformation step are the neutral, functionalised alkyl methyl methylphosphonate esters (R*Me(Me)PO_3) and the corresponding [EMIM]X by-product. Table 1 gives examples using different alkylating agents R*–X together with the reaction conditions and the obtained yields.

The formation of the alkyl methyl methylphosphonate esters was monitored by ^{31}P- and ^{1}H-NMR. The $[Me(Me)PO_3]^-$ ion of the starting IL gives rise to a peak at 18–20 ppm in the ^{31}P-NMR spectrum, whereas the ester product R*Me(Me)PO_3 shows its peak in the ^{31}P-spectrum

Department of Chemical and Bioengineering, Friedrich-Alexander-Universität Erlangen-Nürnberg, Egerlandstr. 3, 91058 Erlangen, Germany. E-mail: wasserscheid@crt.cbi.uni-erlangen.de; Tel: +49 9131 8527420

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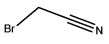
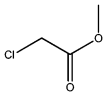
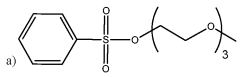
Table 1 Alkylation of [EMIM][Me(Me)PO_3] with different alkylating agents R*–X to form the corresponding neutral esters

Entry	R*–X[a]	Resulting ester	Yield/%
1		AcNMe(Me)PO_3	42
2		MeAcMe(Me)PO_3	74
3	C_4H_9–Br	ButylMe(Me)PO_3	85
4	C_8H_{17}–Br	OctylMe(Me)PO_3	89
5		(MeEG$_3$)Me(Me)PO_3	87
6	$C_{12}H_{25}$–I	DodecylMe(Me)PO_3	92

[a] R*–X was prepared according to Kuhlmann *et al.*[6] Reaction conditions: entry 1: 25 °C, 5 h; entries 2 and 5: 25 °C, 12 h; entry 3: 50 °C, 20 h; entry 4: 60 °C, 20 h; entry 6: 75 °C, 36 h.

at 34–36 ppm. Among the applied alkylation agents R*–X, the alkyl halides with longer alkyl chains were less reactive than those with shorter ones. As expected, the use of alkyl iodides and alkyl bromides resulted in faster transformation compared to the reaction with alkyl chlorides. Isolation of the formed esters R*Me(Me)PO_3 was straightforward by extracting the reaction mixture of the alkylation reaction with diethyl ether. All esters R*Me(Me)PO_3 were obtained after solvent removal in a completely halide-free quality (confirmed by Ag[NO_3] test). The stoichiometric by-product [EMIM]X (X = Cl^-, Br^-, I^-, and [Ph-SO_3]$^-$) could be isolated from the reaction mixture by crystallisation (after cooling in the case of X = Br^- and I^-) and represents itself a valuable ionic liquid material.

It is another remarkable finding of our research that the so obtained esters R*Me(Me)PO_3 exhibit an alkylation strength suitable to quaternise amines to form new ionic liquids with the functionalised group R* attached to the phosphonate ion. This is not a trivial fact, as—for example—carboxylate esters are also obtainable by alkylation of carboxylate ionic liquids.[16] However, the latter cannot be used as alkylating agents. Thus, by reacting the different esters R*Me(Me)PO_3 of Table 1 with ethylimidazole, the corresponding [EMIM] ionic liquids were prepared (for reaction conditions see Table 2; for details on the synthesis see ESI†).

While [EMIM][AcN(Me)PO_3] and [EMIM][MeAc(Me)PO_3] were obtained as pure compounds, the reaction with the phosphonate esters of entries 3–6 (Table 1) afforded defined product mixtures under the applied quaternisation conditions (Scheme 2). For these phosphonate esters also a small part of the functionalised substituent of the alkylating agent was transferred to ethylimidazole, next to the more reactive methyl group. Scheme 2 shows the observed behaviour for R* being an alkyl or ethylene glycol ether group.

The obtained binary mixtures of two different ILs are well defined and may find applications as mixtures *e.g.* in tribology applications. From a synthetic perspective, however, we were interested to develop routes to a large range of pure [R*-methylphosphonate]$^-$ ionic liquids. This requires a selective transfer of the alkyl rest which can be realised if (a) the two alkyl ester groups are very different in their reactivity (see examples 1 and 2 in Table 1) or (b) if the two rests are the same. Following approach (b), we subjected the binary IL mixtures obtained in the first alkylating step to another S_N2 substitution reaction (Scheme 3).

The so obtained neutral phosphonate esters (in relation 90 : 10) were distilled (T = 160 °C, p = 1 bar) to yield the pure alkylating agent R^*_2(Me)PO_3. Obviously, by using R^*_2(Me)PO_3 in the quaternisation of different amines, pure ionic liquids were obtained. However, the latter carry the alkyl group functionality R* in both the cation and the anion (detailed synthetic protocols are given in the ESI†). For comparison of the physico-chemical properties we synthesised in addition the ionic liquids [EMIM][Me(Me)PO_3] and [OMIM][Oc(Ph)PO_3] by reacting the commercially available dimethyl methylphosphonate and dioctyl phenylphosphonate esters with *N*-ethylimidazole and *N*-methylimidazole, respectively. It was found that the alkylating power of the symmetrical phosphonate ester decreases with increasing length of the alkyl residue as found for the asymmetric phosphonate esters. The reaction conditions were adjusted accordingly to realise full conversion. Whereas the methylation reaction by the AcNMe(Me)PO_3 ester (Table 1, entry 1) required acetonitrile as a solvent and 90 °C for 20 h, the alkylation using the dodecyl methyl methylphosphonate ester required a reaction temperature of 160 °C for three days under solventless conditions. Table 2 displays important physico-chemical properties of the obtained phosphonate ionic liquids.

In accordance to the trends found for functionalised alkylsulfate ionic liquids, the density decreases with longer alkyl substituents and increases with oxygen or nitrogen containing functionalisations. The viscosity data demonstrate a strong influence of the functionalisation with the ethylene glycol functionalised ionic liquid showing the lowest viscosity at 20 °C, even lower than [EMIM][Me(Me)PO_3]. The ILs prepared in this study are characterised by reasonable thermal stabilities with values between 216 and 281 °C. The same temperature range was recently reported also for the short-chain, non-functionalised phosphonate ILs.[7] Most of the synthesised phosphonate systems show glass transition temperatures of −50 to −70 °C, only the C_{12}-substituted salt shows a melting point around 60 °C.

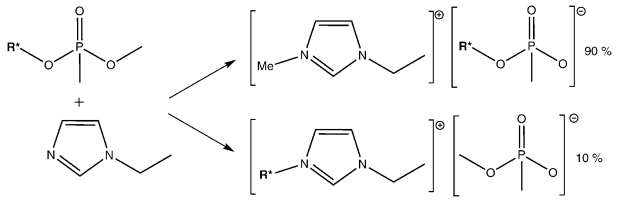
Very remarkably, the hydrolytic stability of the investigated phosphonate ionic liquids was found to be very high. By heating the IL for 5 h in excess water at 100 °C (reflux), no changes in the NMR spectra were observed for all ILs except for [EMIM][MeAc(Me)PO_3]. In this latter case, there was also no hydrolytic reaction at the phosphorous observed but cleavage of the carboxylic ester to form the corresponding acid functionality (for details see ESI†).

In conclusion, our paper presents a new and very general synthetic route to long-chain and functionalised phosphonate esters and the corresponding ionic liquids. The key-step in this method is the S_N2 reaction of a phosphonate ionic liquid with a suitable alkylating agent R*–X to form the neutral esters R*Me(Me)PO_3 or R^*_2(Me)PO_3. These esters can be isolated by extraction or distillation and can serve as alkylating agents to quaternise amines or phosphines. The obtained, functionalised phosphonate salts are free of halogen impurities and display interesting physico-chemical properties including a wide liquid range, relatively low viscosities (taking into account their size and molecular weight) as well as reasonable thermal and very good hydrolytic stability. We anticipate for these new ionic

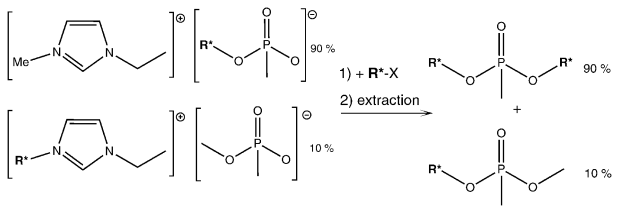
Table 2 Synthesised phosphonate ionic liquids and their properties

Entry	Ionic liquid	ρ^a/g mL^{-1}	η^a/mPa s	T_g/°C	T_{dec}/°C
1	[EMIM][AcN(Me)PO_3]^a	1.21	167	−62.8	236
2	[EMIM][MeAc(Me)PO_3]	1.23	331	−54.7	216
3	[EMIM][Me(Me)PO_3]	1.17	163	−70.1	270
4	[BMIM][Bu(Me)PO_3]	1.07	362	−73.2	253
5	[OMIM][Oc(Me)PO_3]	0.99	465	−60.1	258
6	[OMIM][Oc(Ph)PO_3]	1.02	579	−60.5	281
7	[($MeEG_3$)MIM] [($MeEG_3$)(Me)PO_3]	1.17	141	−70.2	243
8	[C_{12}MIM][C_{12}(Me)PO_3]	Solid		59.5^b	261

^{a} Measured at 25 °C. ^{b} Melting point; water content of the ionic liquids as specified in the ESI.†



Scheme 2 Synthesis of mixed alkyl methylphosphonate ionic liquids by direct alkylation of ethylimidazole with R*Me(Me)PO_3 (R* = alkyl, ethylene glycol ether).



Scheme 3 Synthesis of dialkyl methylphosphonate esters from alkyl methylphosphonate ionic liquids.

liquid structures interesting applications in separation technologies (*e.g.* liquid–liquid extraction), lubrication and carbohydrate chemistry.

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